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| EXAMINER | |
|---|---|
| DIRAMIO, JACQUELINE A | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/530,464 | NYLESE, TARA | |
| | Examiner | Art Unit | |
| | JACQUELINE DIRAMIO | 1641 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *21 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,10,11,15,16,18-21 and 25-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,10,11,15,16,18-21 and 25-29* is/are rejected.

7)☒ Claim(s) *10 and 20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 April 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Status of the Claims*

1. Applicant's amendments to claims 1, 10, 11, 19, 20 and 25 are acknowledged, as well as the cancellation of claims 12 – 14 and 17.

2. Currently, claims 1, 10, 11, 15, 16, 18 - 21 and 25 - 29 are pending and under examination.

### *Withdrawn Rejections*

3. The finality of the previous office action mailed January 15, 2008 is withdrawn in view of Applicant's arguments presented in the Appeal Brief filed June 12, 2008.

4. Further, all previous rejections of the claims under 35 U.S.C. 102(e) and 103(a) are withdrawn in view of Applicant's arguments filed June 12, 2008 and amendments filed October 21, 2008.

### *Response to Arguments*

5. Applicant's arguments, see p8-31 of the Appeal Brief, filed June 12, 2008, with respect to the rejection(s) of the claim(s) under 35 U.S.C. 102(e) and 103(a) have been fully considered and are persuasive. In particular, Applicant argues that the previous rejection of claims 1, 20, 21, 25 and 29 under 35 U.S.C. 102(e) as being anticipated by Toranto et al. (US 2003/0175992) is an error given that the Toranto et al. reference fails to teach multiple unitary test device, wherein each unitary test device

includes a plurality of regions, each responsive at a different sensitivity level to indicate presence of the analyte in the source. Further, Applicant argues that the previous rejection of claims 10 – 16, 19 and 28 under 35 U.S.C. 103(a) as being unpatentable over Boehringer et al. (US 98/39657) in view of Toranto et al. is in error because it would not have been obvious to combine these references in order to arrive at Applicant's claimed invention given that (1) Boehringer et al. fail to teach the "bringing a second sample from the source at a second time subsequent to providing the first sample" in order to provide "information about a change in analyte concentration present in the source between the two times;" and (2) Toranto et al. fail to teach multiple test units, wherein each test unit defines multiple measurably distinguishable sensitivity levels each indicative of a different amount of analyte in the source. These arguments have been found to be persuasive. Therefore, the rejections have been withdrawn.

6. In addition, Applicant's arguments (see p8-11) filed October 21, 2008 have been found persuasive with respect to various references discussed (i.e. O'Brien [US 4,904,605], Becket [US 5,710,372], and Hochstrasser (US 4,059,407]), wherein Applicant argues that the amendments to the claims, which require either antigen or antibody binding or a ligand recognition system, are not taught by these various references. However, upon further consideration, a new ground(s) of rejection is made and presented below.

## NEW GROUNDS OF REJECTION

### *Claim Objections*

7. Claims 10 and 20 are objected to because of the following informalities:

Claim 10, line 28, recites the term "the first sample," which should in fact be "the second sample," as this is what sample this recitation is actually referring to.

Claim 10, lines 31-32, recites the terms "the first test device" and "the second test device," which should be "the first test unit" and "the second test unit," respectively, in order to remain consistent with the previous recitations for these test units.

Claim 20, lines 14-16, recites the phrase "allowing comparison of responses among regions on different test units based levels of association of a detector reagent with a capture reagent," which recites incorrect grammar and should perhaps include the term "on" after the term "based."

Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 19 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 19, which is dependant on claim 10, recites the phrase "the step of defining multiple measurably distinguishable sensitivity levels," which lacks antecedent basis due to the amendments to claim 10.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claims 1, 10, 11, 15, 16, 19 – 21, 25, 28 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Catt et al. (US 6,403,380) in view of Boehringer et al. (WO 98/39657).

Catt et al. teach a method for determining, between two times, a change in a level of concentration of an analyte present in a source, the method comprising:

providing multiple unitary test devices;

bringing a first sample from the source into contact with a first of the unitary test devices at a first time to induce, at the first time, a visually observable response on the first test device based on the source containing a minimum level of analyte concentration;

subsequently bringing a second and different sample from the same source into contact with a second of the unitary test devices at a second time to induce at the second time, a visually observable response on the second test device based on the source containing a minimum level of analyte concentration; and

comparing a visually observable response induced in the first test device at the first time directly with a visually observable response induced in the second test device at the second time to provide information about a change in the level of analyte concentration between the two times (see column 4, lines 28-67; column 5, lines 1-67; column 6, lines 1-9; column 7, lines 42-67; and column 8, lines 1-4).

However, Catt et al. fail to teach that each of the unitary test devices include a plurality of regions, each region responsive at a different sensitivity level to indicate the presence of the analyte in the source, wherein the response in one or more regions is determined based on capillary flow of said sample from a sample receiving region on each of the test devices to one or more of the plurality of regions on the same test device and the response on the device is based on an amount of binding of an antigen and an antibody to form complexes.

Boehringer et al. teach a device and method for determining analyte concentration in a test sample. The method comprises providing a lateral flow device comprising a sample receiving zone, and one or more serially oriented capture zones, wherein the one or more capture zones are responsive at a different sensitivity level to indicate the presence of the analyte in the test sample. Sample is applied to the sample receiving zone and allowed to migrate by capillary action to each of the one or more

capture zones. Each capture zone is capable of providing a visually observable response, based on specific binding, including antigen-antibody binding, wherein a pattern of visually observable responses is created out of the one of more capture zones, which can be correlated to the analyte concentration in the test sample, thereby allowing for visually quantifying the amount of analyte in the sample (see Figure 1; p4, lines 22-38; p5, lines 1-2; p6, lines 15-19; column 7, lines 13-32; p12, lines 1-38; p13, lines 1-38; p14, lines 1-29; p15, lines 3-32; and Tables 1-3 on p41).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include with the method of Catt et al. a plurality of regions on each of the test devices, wherein each region is responsive at a different sensitivity level, as taught by Boehringer et al. because Boehringer et al. teach the benefit of providing a lateral flow device with a plurality of capture zones, wherein each capture zone is responsive at a different sensitivity level to an analyte present in a sample, in order to create a pattern of visually observable responses out of the one of more capture zones, which can be correlated to the analyte concentration in the test sample, thereby allowing for visually quantifying the amount of analyte in the sample.

With respect to Applicant's claim 10, Catt et al. teach a method for monitoring changes in analyte level of a source, comprising:

providing first and second test units,

the first test unit being responsive to the presence of analyte in the source;

the second test unit being responsive to the presence of analyte in the source;

providing a first sample from the source at a first time;

bringing the first sample into contact with the first test unit to provide an indication as to whether analyte is present in the first sample;

providing a second sample from the source at a second time subsequent to providing the first sample; and

bringing the second sample into contact with the second unit to provide an indication as to whether analyte is present in the second sample, wherein a difference between visually observable responses induced in the first test unit at the first time and induced in the second test unit at the second time provides information about a change in the level of analyte concentration present in the source between the two times (see column 4, lines 28-67; column 5, lines 1-67; column 6, lines 1-9; column 7, lines 42-67; and column 8, lines 1-4).

However, as discussed above, Catt et al. fail to teach that the first and second test units comprise lateral flow devices each of the type which includes a receiving zone for fluid samples separated from two or more regions, each region responsive to analyte migrating from the receiving zone by capillary flow into the region, the two or more regions on each test unit defining multiple measurably distinguishable sensitivity levels each distinguishable sensitivity level indicative of a different amount of analyte in the source, wherein the first and second test units include first and second regions of

measurably distinguishable sensitivity levels that are responsive by binding antigen and antibody in order to identify presence of analyte in the source.

Again, as discussed above, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include with the method of Catt et al. a plurality of regions on each of the test devices, wherein each region is responsive at a different sensitivity level, as taught by Boehringer et al. because Boehringer et al. teach the benefit of providing a lateral flow device with a plurality of capture zones, wherein each capture zone is responsive at a different sensitivity level to an analyte present in a sample based on antigen-antibody binding, in order to create a pattern of visually observable responses out of the one of more capture zones, which can be correlated to the analyte concentration in the test sample, thereby allowing for visually quantifying the amount of analyte in the sample.

With respect to Applicant's claim 11, Boehringer et al. teach that test unit can include a second capture line responsive to presence of the second level of analyte and the step of bringing the sample into contact with the test unit includes providing said second capture region an opportunity to indicate the presence of analyte in the sample at at least the second sensitivity level (see Figure 1; p4, lines 22-38; p5, lines 1-2; p6, lines 15-19; column 7, lines 13-32; p12, lines 1-38; p13, lines 1-38; p14, lines 1-29; p15, lines 3-32; and Tables 1-3 on p41).

With respect to Applicant's claims 15 and 16, Boehringer et al. teach that the test unit can include forming thereon at least three capture lines each responsive to the presence of the analyte in the source at a different of the multiple distinguishable

sensitivity levels (see Figure 1; p4, lines 22-38; p5, lines 1-2; p6, lines 15-19; column 7, lines 13-32; p12, lines 1-38; p13, lines 1-38; p14, lines 1-29; p15, lines 3-32; and Tables 1-3 on p41).

With respect to Applicant's claim 19, Boehringer et al. teach that the step of defining the multiple measurably distinguishable sensitivity levels each indicative of a different amount of analyte in the sample is accomplished by forming at least the first and second capture lines (see Figure 1; p4, lines 22-38; p5, lines 1-2; p6, lines 15-19; column 7, lines 13-32; p12, lines 1-38; p13, lines 1-38; p14, lines 1-29; p15, lines 3-32; and Tables 1-3 on p41).

With respect to Applicant's claim 20, Catt et al. teach a method for monitoring changes in analyte level of a source, comprising:

providing two or more test units;

bringing a first sample from the source into contact with a first of the test units to indicate whether the analyte is present in the sample at at least one level; and

on an occasion subsequent to providing the first sample, bringing a second sample from the source into contact with a second of the units to indicate whether the analyte is present in the second sample at at least one level,

wherein different indications on different test units provide evidence as to whether there has been a change in analyte level subsequent to providing the first sample (see column 4, lines 28-67; column 5, lines 1-67; column 6, lines 1-9; column 7, lines 42-67; and column 8, lines 1-4).

However, as discussed above, Catt et al. fail to teach that the two or more test units include multiple regions positioned thereon to receive analyte by capillary flow from a receiving zone, each region in each unit responsive to the presence of analyte in the source at a sensitivity level measurably distinguishable from another region in the same test unit, wherein two or more regions on each unit are responsive components in a ligand recognition system to provide different indications of analyte level allowing comparison of responses among regions on different test units based on levels of association of a detector reagent with a capture reagent resulting from migration of analyte from an associated receiving zone to the regions by capillary flow.

Again, as discussed above, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include with the method of Catt et al. a plurality of regions on each of the test devices, wherein each region is responsive at a different sensitivity level, as taught by Boehringer et al. because Boehringer et al. teach the benefit of providing a lateral flow device with a plurality of capture zones, wherein each capture zone is responsive at a different sensitivity level to an analyte present in a sample based on antigen-antibody binding, in order to create a pattern of visually observable responses out of the one of more capture zones, which can be correlated to the analyte concentration in the test sample, thereby allowing for visually quantifying the amount of analyte in the sample.

With respect to Applicant's claim 21, Boehringer et al. teach that the device is prepared by adhesively mounting the various zones and/or regions to a substrate (see p39, lines 8-37).

With respect to Applicant's claim 25, the limitations of this claim are discussed above with respect to Applicant's claim 20.

With respect to Applicant's claims 28 and 29, Catt et al. teach that the step of providing the two or more test units includes forming the test units separate and apart from one another (see column 5, lines 52-67).

10. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Catt et al. (US 6,403,380) in view of Boehringer et al. (WO 98/39657), as applied to claims 10 and 16 above, and further in view of Cole (US 6,656,745).

The Catt et al. and Boehringer et al. references, which were discussed in the 103(a) rejection above, fail to teach that each of the regions of the first test unit is responsive to substantially the same level of analyte as one of the regions of the second.

Cole teaches a device and method for multi-level, semi-quantitative immunodiffusion assay. The device utilizes a plurality of binding zones wherein the concentration of binding agent immobilized determines a sensitivity of a given binding zone. Individual binding zones can be reactive for pre-determined levels of analyte in a sample, i.e. each binding zone has a specified concentration of binding reagent. Therefore, the binding zones allow for testing of an analyte over a broad range of concentration. The device normally involves a three-binding zone device or "tri-level test." The number of levels can be tailored in combination with the concentration of binding reagents to alter the sensitivity of the semiquantitative analysis depending on the particular application or desired precision. The device can detect for the presence

or absence of the analyte, i.e. by determining trace levels of the analyte, as well as the semiquantitative amount of analyte present. Thus, the device is beneficial to screen for detection and progress of a particular medical condition, e.g. one threshold level can indicate that the condition is at a preliminary stage, whereas another threshold amount can indicate that the condition is in an advanced state. Such devices are beneficial for testing of analytes that occur in a range, such as prostate specific antigen (PSA) or pregnancy hormone (HCG), whose concentration range determines what, if any medical action is necessary (see column 5, lines 16-67; column 6, lines 7-48; and column 7, lines 16-50).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to create the regions of the first unit to be responsive to substantially the same level of analyte as only one of the regions of the second unit of Catt et al. and Boehringer et al. in order to allow for testing of an analyte over a broad range of concentration as taught by Cole because Cole teaches the benefit of semiquantitative testing of analytes that occur in a range, such as prostate specific antigen (PSA) or pregnancy hormone (HCG), whose concentration range determines what, if any medical action is necessary.

11. Claims 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Catt et al. (US 6,403,380) in view of Boehringer et al. (WO 98/39657), as applied to claim 25 above, and further in view of O'Connor et al. (US 2003/0124737).

Catt et al. and Boehringer et al. further fail to teach that the devices are configured to indicate presence of chorionic gonadotrophin, wherein the sample is taken on the second occasion as least one day, or at least 72 hours, after the first occasion.

O'Connor et al. teach a method of predicting pregnancy outcome by determining the amount of molecular isoforms of hCG (human chorionic gonadotropin) in a sample. The various levels of hCG isoforms in blood and urine samples from a pregnant woman change depending on the day or month. In particular, the level of certain hCG isoforms in blood and urine samples at various points of the pregnancy have been found to possibly indicate the cause of early pregnancy loss (see Figures 6, 7, and 9 - 11; and paragraphs [0008]-[0010], [0043], [0060], [0061], [0067], [0074], and [0075]).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include with the method of Catt et al. and Boehringer et al. the change in concentration of chorionic gonadotropin over a certain period of time as taught by O'Connor et al. because O'Connor et al. teach the importance of measuring hCG (chorionic gonadotropin) levels in blood and urine samples from pregnant women because the concentration levels of various isoforms of hCG in the blood and urine samples change over time, and it has been found that the level of certain hCG isoforms at various points of the pregnancy may indicate the cause of early pregnancy loss.

***Conclusion***

12. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JACQUELINE DIRAMIO whose telephone number is (571)272-8785. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jacqueline DiRamio/
Examiner, Art Unit 1641

/Bao-Thuy L. Nguyen/
Primary Examiner, Art Unit 1641
November 7, 2008